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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/671,242	09/24/2003	Ann M. Lees	10797-004006	7827

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/671,242	LEES ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *1-24 and 37-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/13/04,11/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

Applicant's election with traverse of Group III, claims 25-36 filed on February 16, 2006 is acknowledged. Applicants also elects antibody as the candidate agent, however upon reconsideration the requirement of election of a candidate agent from claim 25 is withdrawn, therefore restriction is not treated as a species election. The traversal is on the ground(s) that claims 37-40 of Group IV merely provide further limitations to claims within Group III, therefore claims of Group III and Group IV should be examined together. This is not found persuasive because inventions III and IV are drawn to different subject matter as shown by different classification. Therefore, a search for the method of identifying a candidate agent that binds to LBP-2 of Group III would not encompass a search of claims drawn to a method for treatment of atherosclerosis using the agent that binds to the LBP-2. Consequently, a search of claims directed method of III and IV together would constitute an undue burden.

The requirement is still deemed proper and is therefore made **FINAL**.

Claims 1-24 and 37-66 are withdrawn under 37 C.F.R. § 1.142(b) from further consideration, as being drawn to a non-elected invention. Therefore, claims 25-36 are under examination.

Objection to Specification

The specification is objected to because the continuing data at page 1 has not been updated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific protein and sequence, does not reasonably provide enablement for all the LDL binding proteins, and any variant/analogs or fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claimed invention is directed to a method for identifying a candidate agent that binds to LBP-2 comprising contacting in vitro a candidate agent and LBP-2 polypeptide or a fragment or analog thereof. The specification, however, only discloses cursory conclusions to support the findings. See the discussion below.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision In re Wands, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those skilled in the art, 7) the predictability or unpredictability of the art and 8) the breadth of the claims.

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

The quantity of experimentation necessary:

In the instant case, the amount of experimentation is enormous since the number of changes from the specific sequence are large, one of skill in the art would have to make and test each one to determine if it had the LDL binding activity of the parent protein. The specification on pages17+ provides a discussion about the fragments/analogs. However, the specification fails to provide any detail as to the structure, size or function of the claimed fragment/analogs.

The amount of direction or guidance presented:

The LBP-2 polypeptide in claims 28 and 31 are directed to an amino acid sequence that binds to LDL and has at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 7 and SEQ ID NO: 43 respectively; are identical to a fragment of at least 10 amino acid residues

of SEQ ID NO: 7 and SEQ ID NO: 43 respectively; or differ by one or more conservative amino acid substitutions from the amino acid sequence of SEQ ID NO: 7 and SEQ ID NO: 43 respectively.

The specification while defining the analogs indicates at page 17, last paragraph that analogs of the invention exhibit at least 80%, preferably 90%, more preferably 95% or most preferably 98% homology with substantially the entire sequence of a naturally occurring LBP sequence, preferably with a segment of about 100 or 50, or 30, or 10, or 5, or 4, or 3 or 2 amino acid residues. However, the specification fails to demonstrate any analog that has at least 80% identity to a portion of the sequence set forth in SEQ ID NO: 7 (claim 28) and SEQ ID NO: 43 (claims 31) which have the LDL binding activity. There is no guidance provided to allow the skilled artisan to predict the portion of the SEQ ID NO: 7 or SEQ ID NO: 43 that would have had at least 80% identity to the claimed peptide sequence fragment.

Also the specification fails to describe or provide guidance about the peptide sequence having identity to a fragment of at least ten amino acid residues of SEQ NO: 7 (claims 28) and SEQ ID NO: 43 (claims 31). It is not clear to a skilled artisan that what is the position of these ten amino acids in relation to the amino acid sequence set forth in SEQ ID NO: 7 and SEQ ID NO: 43. Although Examples 8 and 9 (pages 47-50) demonstrate the binding of LBP-2 (full length) and LDL by Affinity Coelectrophoresis Assay (ACE), this is not demonstrative of any analogs that are claimed in claims 28 and 31. For these reasons it would require undue experimentation to make the claimed invention.

The specification indicates at page 18-19 and in Table 1 that preferred analogs include LBP or biologically active fragments thereof whose sequence differ from the wild type sequence by one or more conservative amino acid substitutions or by one or more non-conservative amino acid substitutions, deletions or insertions which do not abolish LBP biological activity. However, the specification fails to provide a variant, which has LBP biological activity. There is no disclosure about the biological activities of these claimed variants. Identification of the full length LDL binding polypeptide (Fig. 7A, SEQ ID NO: 43 and Fig. 7B, SEQ ID NO: 7) is described (see specification page 6 and 11) and exemplified in the specification (Example 8 and 9 LBP-1, LBP-2 or LBP-3), however the specification fails to provide any discussion of a variant of polypeptide of SEQ ID NO: 7 and SEQ ID NO: 43 that retains the activity of the full length

polypeptide of SEQ ID NO: 7 and SEQ ID NO: 43. The amount of guidance presented is limited to the exact sequence. No discussion is present as to where the changes might be made to SEQ ID NO: 7 and SEQ ID NO: 43. An example of desirable guidance for a LDL binding protein would be disclosure of the binding domain, which is not present. There is no guidance as to how the functional fragments and variants of the claimed nucleic acid encoding the protein can be generated. The specification has provided no guidance to enable one of ordinary skill in the art to determine the positions in the protein, which are tolerant to change (e.g., by amino acid deletions, insertions or substitutions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active variants that may be constructed, because no specific guidance has been given in the specification.

The presence or absence of working examples:

The working examples are exclusively drawn to making one full-length LDL binding protein (LBP-1, LBP-2 or LBP-3) and characterizing cDNAs encoding the full-length protein (Examples 8, 9), however, the specification does not provide a working Example that demonstrates the claimed method.

The nature of the invention:

The scope of the claims include numerous structural variants. The specification does not disclose what might be considered a "LDL binding" variants of the claims 28, 29 and 31 or provide any example of the same.

The predictability or unpredictability of the art:

The nature of the variation makes it entirely unpredictable what might be considered a variant before the isolation of such a sequence has actually taken place. The effect of one or a few conservative substitutions might be somewhat predictable, if the active areas of the molecule were known, but more changes than that are less predictable.

The breadth of the claims:

The breadth of the claims is very broad and encompasses an unspecified number of variants regarding the polypeptide of SEQ ID NO: 7 and SEQ ID NO: 43 as biological active variants. Given the breadth of the claims in the invention, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to make and use the mutants/fragments/variants/analogs of broadly claimed group of LDL binding proteins. Such teachings are absent in the specification. The scope of the claims includes fragments, variants, analogs and mutants of polypeptide. However the specification does not provide the information on the structure and function of the claimed variants of the said polypeptide. The number of changes to result in a sequence with 80% identity to the starting sequence would, of course, be 20 changes per hundred amino acids. The effects on function of this many changes is clearly unpredictable. Finally, these claims are very broad in the sense that a vast number of different proteins fall within the scope of the claims.

For these reasons, it would require undue experimentation for one of skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 25-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is rejected as being indefinite because it lacks essential steps as claimed in the method for identifying a candidate agent that binds to LBP-2. No method steps are recited to demonstrate the claimed effect.

Claims 25, 28-32, 34-36 are indefinite because of the use of the term "LBP-2." The full spelled out words should precede an acronym/abbreviation. Claims 26, 27 and 33 are included in

the rejection because they depend from rejected claims and do not correct the deficiency of the claims from which they depend.

Claims 28 and 31 are indefinite because of the use of the term "LDL." The full spelled out words should precede an acronym/abbreviation.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00 am-7:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita Mitra, Ph.D.
April 15, 2006

JON WEBER
SUPERVISORY PATENT EXAMINER